Abstract

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Abstract: DESCRIPTION (provided by applicant): G protein-coupled receptors (GPCRs) represent the largest family of transmembrane signaling molecules in the human genome. They are also the target of more than 50% of drugs on the market today. Although they are best known for their interactions with G proteins, another protein named arrestin is recognized as being as potentially an important mediator of GPCR actions as the G proteins themselves. Arrestins bind with high selectivity to the ligand-bound, phosphorylated form of GPCRs, where they mediate receptor trafficking and the scaffolding of signaling molecules, such as MAP kinases. We have developed an in vitro method to reconstitute the GPCRarrestin interaction using only a phosphorylated peptide representing the carboxy terminus of the receptor. This bead-based method is ideally suited to high throughput screening for the purpose of identifying small molecules that disrupt the arrestin-GPCR interaction. Such molecules will serve as important probes and reagents for the further dissection of the functions of arrestins in vivo. They may also serve as the basis for the development of therapeutic agents that modulate the activity of GPCRs.

Thesaurus Terms:
High throughput screening, G protein-coupled receptors, GPCR, arrestin, receptor trafficking, scaffolding of signaling molecules, MAP kinases, GPCR-arrestin interaction, phosphorylated peptide, bead-based method

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